

CARDIOVASCULAR MEDICINE

Role of echocardiography in the evaluation of syncope: a prospective study

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Objective: To study the role of echocardiography in the stepwise evaluation of syncope.

Design: A prospective observational study with an 18 month follow up.

Setting: University teaching hospital providing primary and tertiary care.

Subjects: 650 consecutive patients with syncope and clinical suspicion of an obstructive valvar lesion, or with syncope not explained by history, physical examination, or a 12 lead ECG, who underwent bidimensional Doppler transthoracic echocardiography.

Main outcome measures: The causes of syncope were assigned using published diagnostic criteria. Echocardiography was considered diagnostic when confirming a suspected diagnosis, or when revealing occult cardiac disease explaining the syncope.

Results: A systolic murmur was identified in 61 of the 650 patients (9%). Severe aortic stenosis was suspected in 20 of these and was confirmed by echocardiography in eight. Follow up excluded further cases of aortic stenosis. In patients with unexplained syncope ($n = 155$), routine echocardiography showed no abnormalities that established the cause of the syncope. Echocardiography was normal or non-relevant in all patients with a negative cardiac history and a normal ECG ($n = 67$). In patients with a positive cardiac history or an abnormal ECG ($n = 88$), echocardiography showed systolic dysfunction (left ventricular ejection fraction $\leq 40\%$) in 24 (27%) and minor non-relevant findings in the remaining 64. Arrhythmias were diagnosed in 12 of the 24 patients with systolic dysfunction (50%), and in 12 of the 64 remaining patients (19%) ($p < 0.01$).

Conclusions: Echocardiography was most useful for assessing the severity of the underlying cardiac disease and for risk stratification in patients with unexplained syncope but with a positive cardiac history or an abnormal ECG.

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Syncope is a common and difficult clinical problem with multiple causes. It prompts many people to seek medical attention and often leads to extensive cardiovascular testing.¹ Echocardiography may be useful in the diagnostic evaluation of patients with syncope, through its ability to diagnose and quantitate obstructive cardiac lesions. It can also provide information about the type and severity of any underlying heart disease, such as left ventricular dysfunction, which may be useful for risk stratification.^{2–4} Nonetheless, the role of echocardiography in the stepwise evaluation of syncope remains unclear^{5–6}—specifically, whether its use is justified in the routine evaluation of all cases of syncope that are unexplained by the history, clinical examination, and 12 lead ECG, or whether it should be targeted toward patients with a positive cardiac history, as recently recommended.⁷ Only retrospective studies are available on this subject.^{8–9} Given that echocardiography requires substantial technical and financial resources, we believe it worthwhile to examine these issues.

Our aims in this study were to make a prospective assessment of the use of echocardiography in confirming obstructive valvar lesions in patients with suggestive clinical findings, in detecting unsuspected cardiac abnormalities that might be related to syncope, and in stratifying patients with unexplained syncope.

METHODS

The data for this study were collected between 1997 and 2000 as part of a population based study of patients with syncope.¹⁰ The study was conducted in the emergency department and the inpatient services of the Hôpital Cantonal, the main teaching hospital of Geneva University School of Medicine and the major primary and tertiary care hospital for the

area. On average, 120 patients are seen daily in the emergency department. All patients aged at least 18 years who presented during the study period with syncope as their main complaint were considered eligible. Syncope was defined as sudden transient loss of consciousness with an inability to maintain postural tone, and with spontaneous recovery. Patients were identified from daily visits to the departments by one of the investigators.

The study was approved by our hospital's institutional review board. The patients' informed consent was obtained before enrolment.

Study design

The study was prospective and observational, with an 18 month follow up. In the emergency department, all patients underwent a standardised evaluation including a complete history, physical and neurological examination, baseline laboratory evaluation, a 12 lead ECG, and testing for orthostatic hypotension. After this evaluation, patients were classified into two groups: (1) those in whom the cause of syncope was established according to disease specific criteria, or where a specific entity causing syncope was suspected by suggestive signs or symptoms but required confirmation by a selected diagnostic procedure; and (2) those in whom the cause of syncope remained undetermined. This latter group underwent serial cardiovascular diagnostic tests which included the following:

- bidimensional Doppler transthoracic echocardiography
- bilateral carotid sinus massage
- prolonged electrocardiographic monitoring
- passive upright tilt testing.

Table 1 Characteristics of study subjects (n=650)

Variable	Cause of syncope established* (n=495)	Unexplained syncope (n=155)	p Value
Age (years)			
Mean (SD)	58 (21)	68 (15)	<0.01
Range	16 to 96	19 to 90	
No ≥75 years	210 (42)	74 (61)	<0.01
Male sex	235 (47)	66 (43)	NS
Syncopal episodes			
First episode	278 (56)	82 (53)	NS
Second episode	114 (23)	30 (19)	NS
Third or more	103 (20)	40 (26)	NS
Last in preceding year	104 (20)	31 (20)	NS
Co-morbid conditions			
CHD	64 (13)	45 (29)	<0.01
Old MI	30 (6)	27 (17)	<0.01
CHF	33 (7)	28 (18)	<0.01
Hypertension	156 (31)	64 (41)	<0.01
Diabetes mellitus	35 (7)	20 (13)	<0.01
PVD	34 (7)	21 (14)	<0.01
COPD	14 (3)	13 (8)	0.02

Values are n (%) unless stated.

*After initial or targeted workup.

CHD, coronary heart disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PVD, peripheral vascular disease.

Electrophysiological studies were performed in selected cases only, based on the recommendations of a consulting cardiologist and on published data.¹¹

Data collection

A full time research physician was available daily in the emergency department and in the hospital ward, and collected baseline data on clinical and physical examination, current drug treatment, cardiovascular risk factors, and the results of all the tests. At the time of admission, the patients were questioned using a standardised protocol recording the number of syncopal episodes, precipitating factors, and the occurrence and duration of prodromal and recovery symptoms, such as those suggesting aortic stenosis (aortic systolic murmur and syncope on exertion with or without chest pain), seizures, stroke or transient ischaemic attacks, and pulmonary embolism.

Diagnostic criteria for cause of syncope

Given the lack of a gold standard against which to validate the performance of various diagnostic tests, we used strict, explicit, and reproducible criteria to establish the causes of syncope.^{7 11}

Diagnostic criteria for non-cardiac causes of syncope

Vasovagal disorder

A diagnosis of vasovagal or situational syncope was accepted only in the presence of premonitory signs (for example, nausea, dizziness) and a precipitating event (such as fear or pain). For patients with unexplained syncope, upright tilt testing was performed on an electrically tilted table with a footplate, according to standardised protocols.^{12 13} We used a 70° tilt angle for 45 minutes without any provocative pharmacological agents. An abnormal test was defined as syncope or presyncope in association with hypotension or bradycardia.

Neurological and psychiatric disorders

Evaluation by a staff neurologist was necessary to classify a neurological disorder (seizure, transient ischaemic attack, or stroke) as the likely cause of syncope. Psychiatric illnesses considered as potential causes of syncope included generalised anxiety disorder, panic and somatisation disorder, and major depression.¹⁴ In all suspected cases, evaluation by a staff psychiatrist was mandatory.

Orthostatic hypotension

After patients had rested in a supine position for five minutes, pulse and pressure measurements were repeated upon standing and after one, two, three, five, and 10 minutes. Hypotension was considered to be the cause of syncope if there was a decrease in the systolic blood pressure of 20 mm Hg or more associated with symptoms.^{7 15} A decrease in blood pressure of 10–20 mm Hg leading to a systolic blood pressure of < 90 mm Hg, with or without symptoms, was also considered a cause of syncope.

Carotid sinus hypersensitivity

Carotid sinus massage was performed on patients in a supine position for up to five seconds, and both sides were tested. Sinus hypersensitivity was considered diagnostic when associated with cardiac asystole lasting for three seconds or more, or with a decrease in systolic blood pressure of ≥ 50 mm Hg with syncope or presyncope.⁷

Diagnostic criteria for cardiac causes of syncope

Transthoracic echocardiographic examination was undertaken using cross sectional Doppler ultrasound. The left ventricular ejection fraction (LVEF) was estimated visually.

Echocardiographic findings considered to be diagnostic of syncope included severe aortic stenosis (mean aortic gradient ≥ 50 mm Hg and valvar area ≤ 0.9 cm²),¹⁶ hypertrophic cardiomyopathy with outflow tract obstruction, severe pulmonary artery hypertension (mean arterial pressure exceeding 30 mm Hg), and left atrial myxoma or thrombus with protrusion and outflow tract obstruction.

Abnormal but non-diagnostic echocardiographic findings included moderate aortic stenosis, mitral stenosis (valvar area ≤ 2 cm²), moderate or severe aortic insufficiency, diffuse or localised ventricular hypokinesia, left ventricular hypertrophy, LVEF ≤ 55%, moderate pulmonary hypertension (mean arterial pressure ≥ 20 and < 30 mm Hg), interatrial septal defect, septum aneurysm, thrombus, or tumour.

Myocardial infarction was implicated only if standard criteria were present and in the absence of other documented causes such as arrhythmias.¹⁷ Pulmonary embolism was diagnosed in the presence of positive Doppler ultrasound, lung scan, or angiography.¹⁸

Arrhythmias (from a 12 lead ECG or a 24 hour Holter test) considered to be diagnostic of syncope included the following:

Table 2 Spectrum of diseases causing syncope in 155 patients with unexplained syncope undergoing cardiovascular testing, and list of tests enabling the diagnosis to be established

Diagnosis	n (%)	Diagnostic tests
Cardiac		
Ventricular tachycardia	12	Holter (8), EPS (4)
A-V block	5	Holter (2), loop recorder (2), EPS (1)
Sinus bradycardia or pause	7	Holter (5), loop recorder (1), EPS (1)
Total	24 (16)	
Non-cardiac		
Vasovagal	14	Tilt test (14)
Hypotension	2	Tilt test (2)
Carotid sinus hypersensitivity	6	EPS (1), tilt test (1), massage (4)
Total	22 (14)	
Unknown	109 (70)	

EPS, electrophysiological testing.

- sinus pause of ≥ 3 seconds or a symptomatic sinus pause of ≥ 2 and < 3 seconds
- sinus bradycardia of ≤ 35 beats/min or symptomatic bradycardia of > 35 and ≤ 40 beats/min
- atrial fibrillation with slow ventricular response (RR interval ≥ 3 seconds)
- supraventricular tachycardia for ≥ 30 seconds at ≥ 180 beats/min or associated with hypotension (systolic blood pressure ≤ 90 mm Hg)
- second degree (Mobitz II) atrioventricular block
- complete atrioventricular block
- sustained ventricular tachycardia (≥ 30 seconds) or symptomatic non-sustained ventricular tachycardia.

A 12 lead ECG was considered abnormal in the presence of any non-diagnostic findings (for example, atrial fibrillation, repetitive premature ventricular contractions, or bundle branch block), except for non-specific ST and T wave abnormalities.

Electrophysiological studies were performed on the basis of current recommendations.^{7,11} Diagnostic findings included a prolonged corrected sinus node recovery time (≥ 550 ms) indicative of sinus node disease; a prolonged HV interval (≥ 100 ms); supraventricular tachycardia of ≥ 180 beats/min or associated with hypotension; sustained ventricular tachycardia; and spontaneous or induced infra-Hisian block.

Follow up

Information regarding new diagnoses explaining syncope, mortality, and recurrences were obtained from the primary physicians and the patients themselves at six month intervals over an 18 month follow up period.

Data analysis

The cardiac history was considered positive in the presence of coronary artery disease (a history of angina pectoris with or without myocardial infarction), documented valvar heart disease, or other types of cardiomyopathy (dilated or obstructive cardiomyopathy, chronic hypertension, or chronic atrial fibrillation).

Echocardiography was considered diagnostic of syncope if it confirmed a diagnosis suspected from the clinical history or physical examination (for example, aortic stenosis), or if it revealed an unsuspected cardiac disorder considered to be the cause of syncope. A low LVEF ($\leq 40\%$), though non-diagnostic, was considered relevant, while other non-diagnostic findings were considered non-relevant.

Table 3 Results of echocardiographic examination in 155 patients with unexplained syncope

Finding	n (%)
Normal	84 (54)
Abnormal but non-relevant	
Aortic stenosis, moderate	9 (6)
Aortic regurgitation, moderate	3 (2)
Mitral stenosis, moderate	2 (1)
Mitral regurgitation, moderate	25 (16)
Mitral regurgitation, severe	5 (4)
Pulmonary hypertension, moderate	14 (9)
Tricuspid regurgitation, moderate	5 (3)
LV dysfunction, moderate (LVEF $>40\%$, $\leq 55\%$)	10 (6)
LVH	25 (15)
Abnormal and relevant	
LV dysfunction, severe (LVEF $\leq 40\%$)	24 (15)

LV, left ventricular; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy.

Statistical testing was performed using SPSS version 9.0 (SPSS Inc, Chicago, Illinois, USA). Variables were compared using the Student *t* test for continuous variables and the χ^2 or Fisher exact test for dichotomous variables. Significance was set at $p < 0.05$ (two sided).

RESULTS

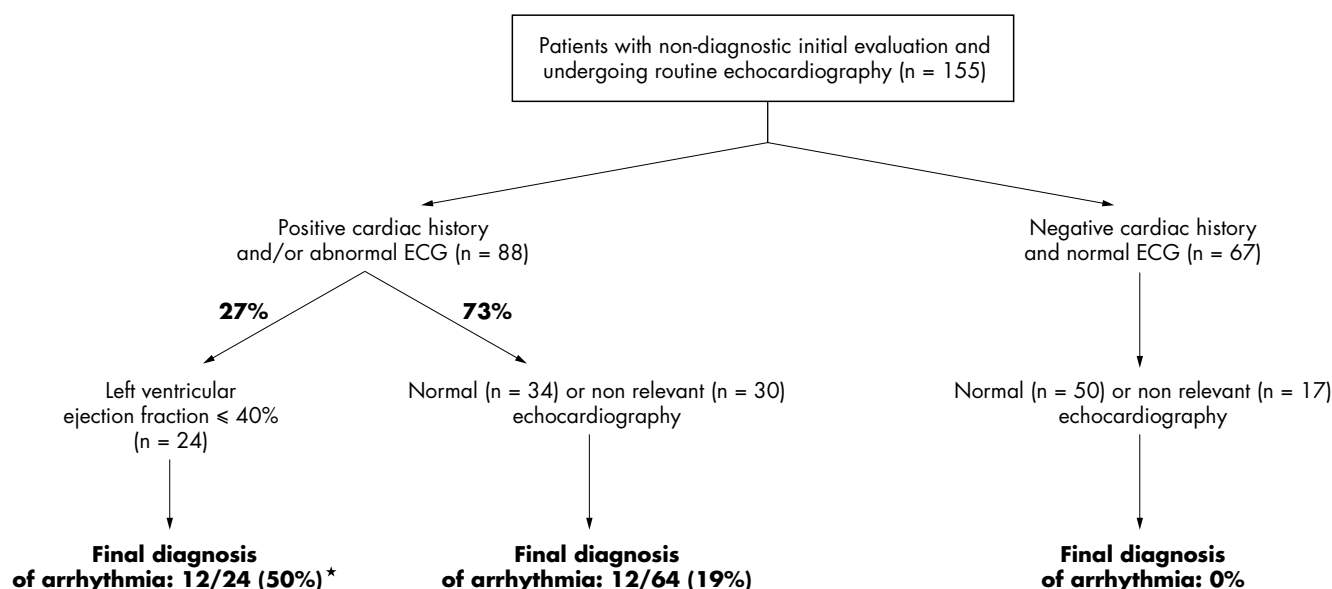
Over a 20 month period, 788 patients were seen in the emergency department with a primary complaint of syncope. Of these, 105 did not complete the standardised evaluation and 33 refused to participate. Thus 650 patients (82%) were enrolled in the study. The patients who did not participate were significantly younger (mean age 55 years) than those who did, and had fewer comorbid conditions. Selected characteristics of the study subjects are shown in table 1.

A probable cause of syncope was assigned after the initial evaluation or targeted diagnostic tests in 495 of the 650 patients (76%). These included vasovagal disorders in 47% ($n = 234$), hypotension in 32% ($n = 156$), neurological and psychiatric disorders in 8% ($n = 41$), cardiac diseases (acute myocardial infarction, pulmonary embolism, or aortic stenosis) in 6% ($n = 29$), arrhythmias in 5% ($n = 26$), and miscellaneous diseases in 2% ($n = 9$). The initial evaluation revealed a systolic murmur in 61 patients (9%) and—on the basis of a suggestive clinical pattern (syncope on exertion with or without chest pain)—aortic stenosis was suspected in 20 of these. Echocardiography within 24 hours confirmed severe aortic stenosis in eight (40%). Follow up over 18 months (achieved in 95%) provided no new diagnoses of severe aortic stenosis.

In all, 155 patients were considered to have unexplained syncope, and a cause of syncope was assigned after cardiovascular testing in 44 of these (28%). Table 2 shows the spectrum of diseases causing syncope in these patients, and the tests that allowed the diagnoses to be established.

All patients had routine echocardiography. Table 3 shows the results of this examination. Over half the echocardiograms (54%) were normal, and overall this procedure did not reveal unexpected cardiac abnormalities that might be diagnostic of syncope. Figure 1 stratifies the results of routine echocardiography as a function of the presence of underlying heart disease on clinical history and baseline ECG. In patients with a negative cardiac history and a normal ECG ($n = 67$), the echocardiogram was either normal ($n = 50$) or non-relevant ($n = 17$). Further diagnostic testing and long term follow up allowed arrhythmias to be excluded in this subgroup. Thus echocardiography in patients with a negative cardiac history and normal ECG was not considered useful.

Eighty eight patients had either a history of cardiac disease or an abnormal ECG. Echocardiography was normal or non-relevant in 64 of these patients (73%), but revealed an



* $p < 0.01$

Figure 1 Results of routine echocardiography as a function of the presence of heart disease and the baseline ECG.

LVEF of $\leq 40\%$ in the remaining 24 (27%). Twelve of these 24 patients (50%) had a final diagnosis of arrhythmias with a low ejection fraction; this diagnosis was assigned to only 19% (12/64) of the patients whose echocardiographic findings were considered non-relevant ($p < 0.01$). Table 4 details the characteristics of patients with a positive cardiac history or abnormal baseline ECG as a function of LVEF.

DISCUSSION

Our results showed that echocardiography was an important initial step in the evaluation of patients with unexplained syncope and with a positive cardiac history or an abnormal ECG. When restricted to these high risk patients, echocardiography provided useful information for assessing the severity of the underlying heart disease and for risk stratification. While echocardiography showed systolic dysfunction—defined as an ejection fraction of $\leq 40\%$ —in 27% of these patients, arrhythmias were diagnosed twice as often when the ejection fraction was low. It is known that clinical recognition of severe systolic dysfunction is unreliable,^{19–21} so this contribution of echocardiography can be considered important.

Recent guidelines stated that routine echocardiography in patients with syncope and no evidence of underlying cardiac

disease was controversial.⁶ In clinical practice, however, this procedure is often ordered in patients with syncope for no obvious reason. Recchia and Barzilai found that echocardiography was done in nearly two thirds of patients admitted to hospital for unexplained syncope,⁸ while Calkins and colleagues found that 67% of the patients had undergone echocardiography as part of their evaluation before referral.²² Our results showed that in patients with a negative cardiac history and a normal ECG, no arrhythmias were diagnosed and echocardiography was useless, detecting only minor structural cardiac abnormalities. Thus it is reasonable to anticipate that restriction of echocardiography to patients having a cardiac history or an abnormal ECG would reduce unnecessary diagnostic testing and thereby decrease costs.

In patients with syncope remaining unexplained by clinical history, physical examination, or 12 lead ECG, routine echocardiography did not reveal occult cardiac diseases, such as severe pulmonary hypertension, that might explain the syncopal event. The most common cardiac abnormalities were moderate mitral regurgitation and left ventricular hypertrophy, which have little relevance in the pathogenesis of syncope. On the other hand, our results showed that in patients with syncope and clinical findings suggestive of obstructive cardiac lesions, targeted echocardiography was

Table 4 Characteristics of patients with a positive cardiac history and/or abnormal baseline ECG as a function of left ventricular ejection fraction

Variable	LVEF $\leq 40\%$ (n=24)	LVEF $> 40\%$ (n=64)	p Value
Age (mean (SD))	75 (7)	73 (11)	<0.01
CAD	18 (75)	27 (42)	<0.01
Previous MI	13 (54)	14 (22)	<0.01
Physical examination in emergency department			
Pulse > 90 beats/min	8 (33)	16 (25)	NS
Third heart sound	4 (17)	0	NS
Pulmonary rales	10 (42)	15 (23)	NS
12 lead ECG			
Old MI	8 (33)	8 (12)	0.03
Left or right BBB	12 (50)	14 (22)	0.04
Multiple PVCs	7 (29)	9 (14)	NS

Values are n (%) unless stated.

BBB, bundle branch block; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PVC, premature ventricular contractions.

useful in confirming the disease and assessing its severity. Although severe aortic stenosis is responsible overall for less than 2% of all cases of syncope (1.2% in this series), the selected application of echocardiography to patients with suggestive symptoms had a high diagnostic yield (40%).

Limitations

Our study had several limitations. First, one problem in the evaluation of syncope is the lack of a gold standard against which the results of diagnostic tests can be assessed. Thus the relation between an abnormal finding during testing and the syncopal event may sometimes be challenged. However, we used restrictive and explicit diagnostic end points⁵⁻⁷ that are currently accepted and have been used in other studies.²³

Second, our sample size of patients with unexplained syncope was relatively small and our population was unselected, which could explain the low diagnostic yield of echocardiography. It can be hypothesised that routine echocardiography performed among a larger, or more selected, cohort of patients could detect occult cardiac diseases such as pulmonary hypertension that might or might not be related to the syncopal episode.

Third, a relatively small proportion of our patients had cardiac arrhythmias; thus our results may not be applicable to patients admitted to referral centres where the prevalence of this disorder is higher.

Finally, electrophysiological testing was not performed in all patients with cardiac diseases. Our indications for this test were, however, based on current recommendations,¹¹ and its diagnostic yield was comparable with that published in a previous report.⁵

Conclusions

Echocardiography is useful for risk stratification—by measuring left ventricular function, a predictor of arrhythmias—only in patients with unexplained syncope and with a positive cardiac history or abnormal ECG. It is also useful for confirming severe aortic stenosis in patients with suggestive signs or symptoms.

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